REMARKS

This in reply to the Office Action mailed 13 April 2010. By this Amendment claims 1, 31, 37, 38, 40 and 41 have been amended. Claims 5, 14, 24 and 28 have been cancelled. New claims 42-47 have been added.

1.0 Interview Summary

The applicant thanks the Examiner for the courtesy of the telephonic interview extended to the applicant's agent on 6 July 2010 respecting this application. The Examiner and applicant's agents reviewed the working examples in the application showing reduction to practice of embodiments of the invention.

2.0 Elections/Restrictions

Withdrawn claims 5, 14, 24 and 28 have been cancelled.

3.0 Specification Objection and Claim Rejections - 35 USC § 112

3.1 Biological Deposit

As set forth in 37 CFR 1.802(b), biological material need not be deposited, *inter alia*, if it is known and readily available to the public or can be made or isolated without undue experimentation. In the present case, it is submitted that applicant's specification provides sufficient guidance on how to produce the claimed invention from publicly available source material.

In particular, the claimed invention relates to sensors comprising first and second oligonucleotide stems and an aptamer operatively connected to such stems. In Section 2.2 of the specification the applicant provides specific guidance on how to acquire and prepare DNA sequences and assemble sensor constructs by annealing mixtures of constituent oligonucleotides. Preparation of aptamers is described, *inter alia*, at page 2, lines 25-33 and in Figure 10 of the application. It is submitted that SELEX methods for generating aptamer sequences specific to a target analyte would be well within the knowledge of a person skilled in the art. Further, DNA synthesis

techniques are well known and the short lengths of nucleic acids required to practice the invention can be chemically synthesized, e.g. by using a commercial synthesizer or by using an in vitro T7 RNA polymerase system, as disclosed in the present specification, e.g. at page 15, line 35 - page 16, line 2.

It is therefore submitted that the written instructions in applicant's patent specification are clearly sufficient to enable a person skilled in the art to reproducibly construct the claimed invention from starting material known and readily available to the public. The Examiner is therefore respectfully requested to withdraw the requirement for a deposit of biological material.

3.2 Written Description

The Examiner has rejected claims 1-4, 6-13, 15-23, 25-27 and 29-41 as failing to comply with the written description requirement set forth in 35 USC § 112, first paragraph. The Examiner is respectfully requested to withdraw this rejection in view of the following comments.

The applicant has amended claims 1, 31, 37, 38, 40 and 41 to indicate that the first and second oligonucleotide stems each comprise a plurality of base pairs capable of permitting charge conduction along a length of said stems. Support for this amendment can be found, *inter alia*, at page 10, lines 8-12 and page 10, lines 28-30 of the specification.

It is submitted that the applicant has set forth in the specification sufficiently detailed, relevant identifying characteristics of the invention such that a person skilled in the art would recognize that the applicant was in possession of the subject matter of the claims as amended. As indicated above, the claimed invention relates to sensors comprising first and second oligonucleotide stems and an aptamer operatively connected to such stems. Binding of an analyte to the aptamer modulates charge transfer between the first and second stems. That is, analyte binding to the aptamer causes the aptamer to change its conformational state resulting in a detectable increase or decrease in charge transfer between the first and second stems.

As will be appreciated by a person skilled in the art, the first and second stems must each be capable of permitting charge transfer. The electrical conductivity of DNA is well-known in the prior art, as indicated, for example at pages 1-3 and page 14, lines 9-22 of the specification. As

indicated at page 1, lines 19-30 of the specification, long-range electron transfer in double-stranded DNA is generally believed to be the result of a multi-step hopping reaction. The consensus view is that a continuous base-stacking throughout the DNA duplex is necessary for efficient charge transfer. Disruptions in base-stacking may impede electrical conduction (specification at page 13). Thus the specific nucleotide sequence of the oligonucleotide stems is not critical so long as the base pairing within the stems permits charge conduction. It is submitted that information that is well known in the art need not be included in the specification: *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991), and that it would be unfair to the applicant to restrict the invention only to sensors having specific nucleotide sequences.

Further, it is submitted that it would not require undue experimentation by a person skilled in the art to identify nucleotide sequences capable of conducting charge. The applicant's specification describes specific methods for both indirectly and directly detecting charge transfer (specification at page 12, lines 10-11). The applicant teaches that charge transfer may be indirectly detected by electrophoretically monitoring DNA strand cleavage (e.g. specification at page 12, line 27 - page 13, line 11 and page 25, lines 18-24) or directly by direct electronic readout (e.g. specification at page 12, lines 13-18). No particular skill or inventive steps and no undue burden would be required to exclude oligonucleotide stems which were incapable of conducting charge.

It is also submitted that it would also be readily within the skill of a person skilled in the art to construct sensors as claimed by the applicant by following the teaching of the applicant's specification. Sensor construction involves preparation of an assembly comprising electrical conductive first and second oligonucleotide stems and an aptamer. Oligonucleotide stems having base pairs capable of permitting charge conduction are described above. As also indicated above, an aptamer specific to a target analyte may be readily created by a person skilled in the art as described, for example, at page 2, lines 25-33 and in Figure 10 of the specification. The sensor construct may then be assembled by annealing constituent oligonucleotide strands (specification at page 24, lines 30-33).

The applicant provides multiple working examples of actual sensors constructed in accordance with the teachings of the specification which are capable of detecting analytes such as adenosine. Such sensors comprise a first oligonucleotide stem (e.g. a first DNA strand); a second oligonucleotide stem (e.g. a second DNA strand); and a receptor capable of binding analyte (e.g.

a high affinity DNA aptamer for detecting the presence of the analyte). With respect to adenosine, as indicated in Example 2.1 of applicant's specification, NMR studies have confirmed that the sensor aptamer, upon binding two molecules of adenosine, undergoes an adaptive folding forming a tightly hydrogen-bonded and stacked helical structure. Further, applicant's Example 2.3 clearly demonstrates that the adenosine-induced folded structure of the aptamer receptor was capable of facilitating charge transfer between the first and second oligonucleotide stems.

Further, the applicant's specification describes embodiments wherein binding of the target analyte to the aptamer results in either a reduction in charge transfer or an increase in charge transfer. For example, in the embodiment of Figures 4(a) and 4(b), the binding of a protein to an aptamer or other protein binding site interferes with the electronic path between the oligonucleotide stems 14, 16 (and hence is detectable as a reduction in charge transfer) (specification at page 17, line 22 - page 18, line 7). As will be appreciated by a person skilled in the art, binding of a protein to an aptamer or other receptor can cause a physical interference or steric clash which alters the base stacking geometry of the stems and hence interferes with the conductive path of the sensor. Alternatively, as shown for example in the embodiments of Figure 11, binding of an analyte, such as adenosine, can cause structural changes in the aptamer element located adjacent to a "disrupted" conduction path which help re-establish base stacking and hence "repair" the conduction path.

The guidelines set forth in MPEP § 2163 state that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

It is submitted that the applicant has described an actual reduction to practice of different embodiments of sensors having the identifying characteristics recited in the claims. It follows from the foregoing that it would be readily apparent to a person skilled in the art that the applicant was in possession of the subject matter of the claims as of the application filing date.

4.0 Double Patenting

In reply to the Examiner's provisional obviousness-type double patenting objection at pages 14-15 of the Office Action, the applicant has entered a terminal disclaimer on co-pending continuation-in-part application serial No. 12/102669. It is submitted that the Examiner should therefore withdraw the provisional obviousness-type double patenting objection in the present application in accordance with MPEP 1400-109.

5.0 Summary

In view of the claim amendments and the above comments the applicant respectfully requests withdrawal of the rejections and allowance of this application. If the Examiner has any questions about this paper, or is not convinced that the claims are in condition for allowance, Applicant requests a personal interview with the Examiner.

Respectfully submitted,

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